06-11-07 C9C

Attorney's Docket No.: 18202-018001 / 1082

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Lin Zhi et al.	Art Unit	: 1623
Patent No.	: 7,214,690	Examiner	: Lawrence E. Crane, Ph.D.
Issue Date	: May 8, 2007	Conf. No.	: 8671
Serial No.	: 10/080,503	Cust. No.	: 20985
Filed	: February 22, 2002		
Title	: TRICYCLIC QUINOLINONE AND TRICYCLIC QUINOLINE ANDROGEN RECEPTOR MODULATOR COMPOUNDS AND METHODS		

Attn: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith are a Request for a Certificate of Correction pursuant to C.F.R. § 1.322 (15 pages), Certificate of Correction Form PTO-1050 (15 pages), a copy of the first page of Venturoli et al., J. Clin. Endocrin. Metab. 84:1304 (1999) (1 page), a copy of the Amendment After Final (41 pages) mailed on 19 May 2006, a copy of the Examiner's Amendment (3 pages) mailed on 31 August 2006, and a return postcard for filing in connection with the above-identified application. Pursuant to 37 C.F.R. § 1.322 for a Certificate of Correction for Office mistakes, no fee is due. However, should it be determined that a fee for filing these papers is required, the Commissioner is authorized to charge Deposit Account No. 06-1050, as stated below:

☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 06-1050. A duplicate of this sheet is enclosed.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 18202-018001 / 1082
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Certificate
JUN 13 2007
of Correction

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I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

Stephanie Seidman

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Higuchi et al.	Art Unit	: 1623
Patent No.	: 7,214,690	Examiner	: Lawrence E. Crane, Ph.D.
Issue Date	: May 8, 2007	Cust. No.	: 20985
Serial No.	: 10/080,503	Conf. No.	: 8671
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Title	: TRICYCLIC QUINOLINONE AND TRICYCLIC QUINOLINE ANDROGEN RECEPTOR MODULATOR COMPOUNDS AND METHODS		

Attn.: Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF REQUEST FOR CERTIFICATE OF CORRECTION

Dear Sir:

Pursuant to 37 C.F.R. § 1.322, the patentee respectfully requests that a Certificate of Correction be issued for the above referenced patent to correct the following errors:

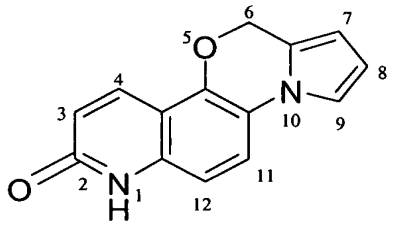
IN THE TITLE PAGES:

In Item [56] References Cited, in OTHER PUBLICATIONS:

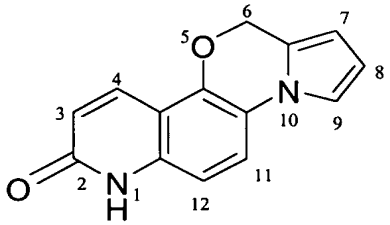
in Venturoli et al., please replace "Prospectiove" with –Prospective–.

IN THE SPECIFICATION:

At column 5, lines 16-25, please replace structure



with the following structure



;

at column 9, line 34, please replace "A R^9" with $-R^9-$; and

at column 31, lines 56-67, please replace structure

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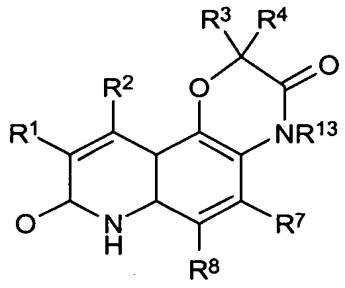
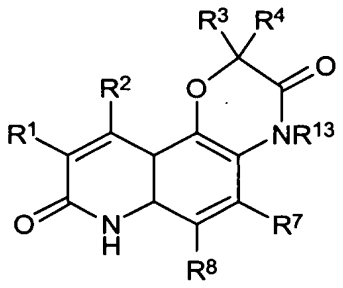
Stephanie Seidman



34

with the following structure

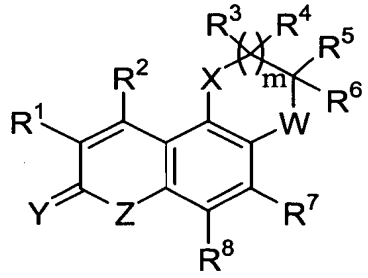


34

IN THE CLAIMS:

Please replace Claims 1, 10, 24, 40, 57, and 58 with the following Claims:

1. A compound having the formula:



(I)

~~OR~~

wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, $\underline{OR^9}$, $S(O)_nR^9$, $NR^{10}R^{11}$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, optionally substituted ~~C_1–C_8alkyl~~ $\underline{C_1$–C_8} alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl,

optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^5 and R^6 each independently is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted C_1–C_8 alkyl, optionally substituted ~~C_1–C_8haloalkyl~~ C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{10} is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{13} is selected from the group consisting of optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_2–C_8 alkenyl, optionally substituted C_2–C_8 alkynyl, optionally substituted C_3–C_8

cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl;

m is selected from the group consisting of 0, 1 and 2;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is O;

Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof; wherein:

the substituents of an optionally substituted group comprise one or more substituents independently selected from among alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyester, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9, $NR^{10}R^{11}$, CF_2CF_3, CH_2CH_2F and CH_2CF_3.

10. The compound of claim 1, wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 cycloalkyl, aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 cycloalkyl, aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 cycloalkyl, aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^5 and R^6 each independently is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 <u>cycloalkyl,</u> aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl and arylalkyl;

R^{10} is selected from the group consisting of hydrogen, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl, arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl and arylalkyl;

R^{13} is selected from the group consisting of C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_2–C_8 alkenyl, C_2–C_8 alkynyl, C_3–C_8 cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl;

m is selected from the group consisting of 0, 1 and 2;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is O;

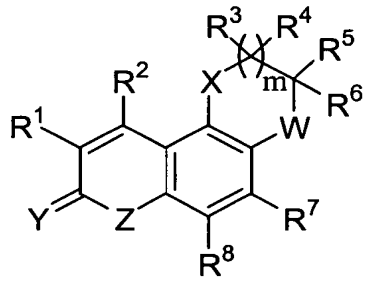
Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof.

24. A compound according to claim 23, wherein R^9 is selected from the group consisting of hydrogen and optionally substituted [[C_3–C_4]] $\underline{C_1\text{–}C_4}$ alkyl.

40. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of formula:



(I)

~~OR~~

wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^5 and R^6 each independently are selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted C_1–C_8 alkyl, optionally substituted ~~C_1–C_8haloalkyl~~ C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8

optionally substituted heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, ~~OR^9, $S(O)_nR^9$~~, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{10} is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{13} is selected from the group consisting of optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_2–C_8 alkenyl, optionally substituted C_2–C_8 alkynyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl;

m is 1;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is O;

Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof; wherein:

the substituents of an optionally substituted group comprise one or more substituents independently selected from among alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl,[[.]] haloalkynyl,[[.]] cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyester, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9, $NR^{10}R^{11}$, CF_2CF_3, CH_2CH_2F and CH_2CF_3.

57. A compound selected from the group consisting of:

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3,4-dimethyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-4-Ethyl-2,3,4,7-tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-~~2,3 4,7~~ 2,3,4,7-Tetrahydro-3-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-4-Allyl-2,3,4,7-tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3,4-Diethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one ;

(3*R*)-4-Allyl-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-isobutyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-3-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-4-methyl-3-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R/S*)-4-Ethyl-2,3,4,7-tetrahydro-3-propyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-3-propyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-4-Ethyl-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Allyl-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-phenyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-phenyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Cyclopropylmethyl-2,3,4,7-tetrahydro-3-phenyl-10-(trifluoromethyl)-8*H*-[1,4]~~oxazino1~~oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Benzyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

2,3,4,7-Tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7-Ethyl-7,7a,8,9,10,10a-hexahydro-1-(trifluoromethyl)-4*H*-cyclopenta-[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-3-isopropoxy-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-~~cyclopenta1~~cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(±)-(2*S*,3*R*)-2,3,4,7-Tetrahydro-2,3-dimethyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(6a*R*)-6a,7,8,9 -Tetrahydro-4-(trifluoromethyl)-1*H*,6*H*-pyrrolo[1',2':4,5][1,4]-oxazino[2,3-*f*]quinolin-2-one;

2,3,4,7-Tetrahydro-2,2,4-trimethyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-8-Chloro-3-ethyl-3,4-dihydro-8-isopropoxy-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-2*H*-[1,4]oxazino[2,3-*f*]quinoline;

(3*R*)-3-Ethyl-3,4-dihydro-8-isopropoxy-8-methoxy-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-2*H*-[1,4]oxazino[2,3-*f*]quinoline;

(±)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(–)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(+)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-4-methyl-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-4-Ethyl-2,3,4,7-tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(-)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(+)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-4-Cyclopropylmethyl-2,3,4,7-tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Cyclopropylmethyl-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-2-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-4-(2-hydroxy-2-methylpropyl)-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

(3*R*)-2,3,4,7-Tetrahydro-3-isobutyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

pharmaceutically acceptable ~~salt~~ salts thereof.

58. A compound selected from the group consisting of:

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(7a*R*,10a*S*)-7-Ethyl-7,7a,8,9,10,10a-hexahydro-1-(trifluoromethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(±)-(2*S*,3*R*)-2,3,4,7-Tetrahydro-2,3-dimethyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(–)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

(+)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

[[a]] pharmaceutically acceptable salts thereof.

REMARKS

A Certificate of Correction (Form PTO-1050) incorporating the above changes is included with this Request. Since the errors appear to be those of the PTO, no fee is due. If it is determined that a fee is due, the Office is hereby authorized to charge the fee to Deposit Account 06-1050.

This Certificate of Correction seeks to correct an obvious spelling error in the "OTHER PUBLICATIONS" section of the References Cited, Item [56] made by the PTO. The amendment to Venturoli et al. seeks to correct a spelling mistake introduced by the PTO by replacing "Prospectiove" with –Prospective–. The basis for this amendment is found on the first page of Venturoli et al., J. Clin. Endocrin. Metab. 84:1304 (1999), a copy of which is herewith attached as evidence.

This Certificate of Correction seeks to correct obvious typographical and grammatical errors in the Specification made by the PTO. The amendment to the structure at column 5, lines 16-25 seeks to replace a nitrogen to carbon double bond with a nitrogen to carbon single bond. This amendment finds basis on page 8, lines 8-10 of the originally filed application, where the structure is correctly presented with a carbon-nitrogen single bond. The amendment to the structure at column 31, lines 56-67 seeks to replace an oxygen to carbon single bond with an oxygen to carbon double bond. This amendment finds basis on page 42, line 2 of the originally filed application, where the structure is correctly presented with a oxygen-carbon double bond.

This Certificate of Correction seeks to correct typographical, spelling, and grammatical errors in the Claims. Claim 1 is amended to correct an error introduced by the PTO at column 79, lines 45-50 by deleting the word "OR" next to formula I. The basis for this amendment is found on page 2, line 8 of the Amendment After Final, mailed on 19 May 2006, a copy of which is herewith attached as evidence. Claim 1 is also amended to correct an error introduced by the PTO at column 79, line 66-67 by inserting list item "OR^9" between "CH_2OR^9" and "$S(O)_nR^9$". The basis for this amendment is found on page 118, line 13 of the originally filed application. Claim 1 is also amended to correct errors introduced by the PTO at column 80, lines 31 and 40 by inserting a space between "C_8" and "alkyl" and between "C_8" and "haloalkyl", respectively. The basis for these amendments are found on page 118, line 18 and on page 119, line 6 of the originally filed application, respectively.

Claim 10 is amended to correct an omission by the PTO at column 82, line 26 by inserting the term –cycloalkyl,– between "C_3-C_8" and "alkyl". The basis for this amendment is found on page 20, lines 20-21 of the Amendment After Final, mailed on 19 May 2006, a copy of which is herewith attached as evidence.

Claim 24 is amended to correct a typographical error introduced by the PTO at column 83, line 55 by replacing the subscript "3" with a subscript "1". The basis for this amendment is found on page 124, line 17 of the originally filed application.

Claim 40 is amended to correct an error introduced by the PTO at column 85, lines 25-30 by deleting the word "OR" next to formula I. The basis for this amendment is found on page 14, line 26 of the Amendment After Final, mailed on 19 May 2006, a copy of which is herewith attached as evidence. Claim 40 is also amended to correct errors introduced by the PTO at column 85, line 67 and at column 86, line 16 by inserting a space between "C_8" and "haloalkyl" and between "OR^9" and "$S(O)_nR^9$", respectively. The basis for these amendments are found on page 137, line 6 and line 21 of the originally filed application, respectively. Claim 40 is also amended to correct punctuation errors introduced by the PTO at column 86, line 56 by deleting a period following "haloalkenyl," and by replacing the period with a comma immediately following list item "haloalkynyl". The basis for these amendments are found on page 17, line 9 of the Amendment After Final, mailed on 19 May 2006, a copy of which is herewith attached as evidence.

Claim 57 is amended to correct a spacing error and an omission by the PTO at column 88, line 34 by replacing the space between numbers "3" and "4" with a comma. The basis for this amendment is found on page 130, line 7 of the originally filed application. Claim 57 is also amended to correct an error introduced by the PTO at column 89, line 27 by deleting the numeral "1" following "oxazino". The basis for this amendment is found on page 132, line 2 of the originally filed application. Claim 57 is also amended to correct an error introduced by the PTO at column 89, line 43 by deleting the numeral "1" following "penta". The basis for this amendment is found on page 132, line 13 of the originally filed application. Claim 57 is also amended to correct an omission by the PTO at column 90, line 31 by inserting the word "and" following the semicolon. This amendment finds basis on page 2 of the Examiner's Amendment to the record, mailed on 31 August 2006, a copy of which is attached herewith as evidence. Claim 57 is also amended to correct a spelling error introduced by the PTO at column 90, line 35 by replacing the word "salt" with "salts". The basis for this amendment is

found on page 2 of the Examiner's Amendment to the record, mailed on 31 August 2006, a copy of which is attached herewith as evidence.

Claim 58 is amended to correct an omission by the PTO at column 91, line 6 by inserting the word "and" following the semicolon. This amendment finds basis on page 2 of the Examiner's Amendment to the record, mailed on 31 August 2006, a copy of which is attached herewith as evidence. Claim 58 is also amended to correct an omission by the PTO at column 90, line 35 by inserting the word "a" immediately proceeding the word "pharmaceutically". The basis for this amendment is found on page 2 of the Examiner's Amendment to the record, mailed on 31 August 2006, a copy of which is attached herewith as evidence.

Accordingly, none of the requested changes constitute new matter. Patentee respectfully requests correction of errors by issuance of a Certificate of Correction.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 18202-018001 / 1082
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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. .: 7,214,690

APPLICATION NO .: 10/080,503

DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

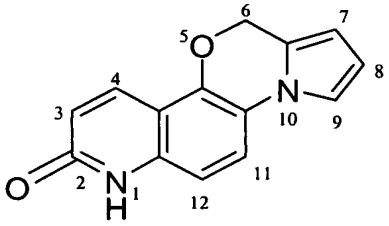
It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE TITLE PAGES:

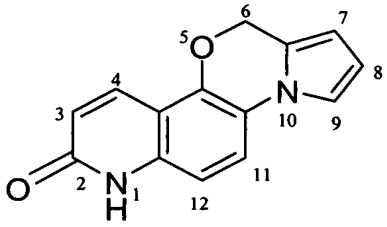
In Item [56] References Cited, in OTHER PUBLICATIONS:
in Venturoli et al., please replace "Prospectiove" with –Prospective–

IN THE SPECIFICATION:

At column 5, line 20, please replace structure

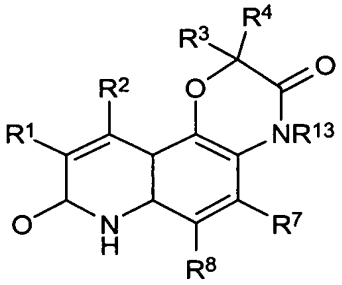


with the following structure



At column 9, line 34, please replace "A R^9" with $-R^9-$

At column 31, line 56-67, please replace structure



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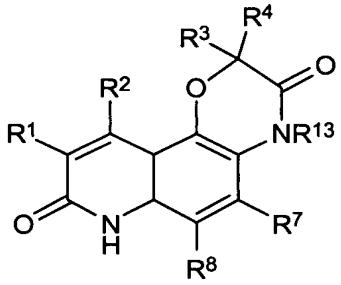
with the following structure



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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. .: 7,214,690

APPLICATION NO .: 10/080,503

DATED .: MAY 8, 2007

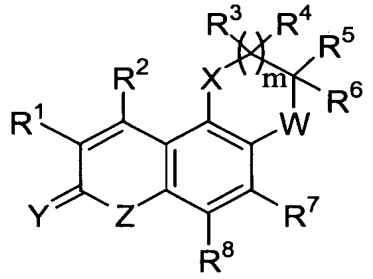
INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE CLAIMS:

Please replace Claims 1, 10, 24, 40, 57, and 58 with the following Claims:

1. A compound having the formula:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

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CERTIFICATE OF CORRECTION

PATENT NO. .: 7,214,690

APPLICATION NO .: 10/080,503

DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^5 and R^6 each independently is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

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PATENT NO. .: 7,214,690

APPLICATION NO .: 10/080,503

DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

R^{10} is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{13} is selected from the group consisting of optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_2–C_8 alkenyl, optionally substituted C_2–C_8 alkynyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl;

m is selected from the group consisting of 0, 1 and 2;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is O;

Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof; wherein:

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. .: 7,214,690

APPLICATION NO .: 10/080,503

DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

the substituents of an optionally substituted group comprise one or more substituents independently selected from among alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyester, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9, $NR^{10}R^{11}$, CF_2CF_3, CH_2CH_2F and CH_2CF_3.

10. The compound of claim 1, wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 cycloalkyl, aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 cycloalkyl, aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 cycloalkyl, aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^5 and R^6 each independently is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_3–C_8 cycloalkyl, aryl, arylalkyl, heteroaryl, C_2–C_8 alkynyl and C_2–C_8 alkenyl;

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. .: 7,214,690

APPLICATION NO .: 10/080,503

DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl and arylalkyl;

R^{10} is selected from the group consisting of hydrogen, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl, arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, aryl, heteroaryl and arylalkyl;

R^{13} is selected from the group consisting of C_1–C_8 alkyl, C_1–C_8 haloalkyl, C_1–C_8 heteroalkyl, C_2–C_8 alkenyl, C_2–C_8 alkynyl, C_3–C_8 cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl;

m is selected from the group consisting of 0, 1 and 2;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is O;

Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof.

24. A compound according to claim 23, wherein R^9 is selected from the group consisting of hydrogen and optionally substituted C_1–C_4 alkyl.

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APPLICATION NO .: 10/080,503

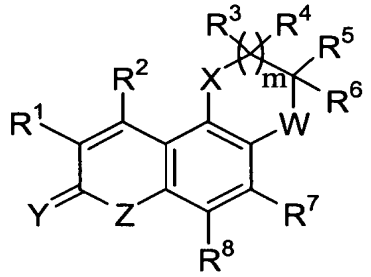
DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

40. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of formula:

(I)



wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

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INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^5 and R^6 each independently are selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted C_2–C_8 alkynyl and optionally substituted C_2–C_8 alkenyl;

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 optionally substituted heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

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DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

R^{10} is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{13} is selected from the group consisting of optionally substituted C_1–C_8 alkyl, optionally substituted C_1–C_8 haloalkyl, optionally substituted C_1–C_8 heteroalkyl, optionally substituted C_2–C_8 alkenyl, optionally substituted C_2–C_8 alkynyl, optionally substituted C_3–C_8 cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl;

m is 1;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is O;

Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof; wherein:

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It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

the substituents of an optionally substituted group comprise one or more substituents independently selected from among alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyester, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9, $NR^{10}R^{11}$, CF_2CF_3, CH_2CH_2F and CH_2CF_3.

57. A compound selected from the group consisting of:

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3,4-dimethyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-4-Ethyl-2,3,4,7-tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-4-Allyl-2,3,4,7-tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

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INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

(3*R*)-3,4-Diethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-4-Allyl-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-isobutyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-3-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-4-methyl-3-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R/S*)-4-Ethyl-2,3,4,7-tetrahydro-3-propyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-3-propyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

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APPLICATION NO .: 10/080,503

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INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-4-Ethyl-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Allyl-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-phenyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-phenyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Cyclopropylmethyl-2,3,4,7-tetrahydro-3-phenyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Benzyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

2,3,4,7-Tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

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APPLICATION NO .: 10/080,503

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INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

(7a*R*,10a*S*)-7-Ethyl-7,7a,8,9,10,10a-hexahydro-1-(trifluoromethyl)-4*H*-cyclopenta-[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-3-isopropoxy-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(±)-(2*S*,3*R*)-2,3,4,7-Tetrahydro-2,3-dimethyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(6a*R*)-6a,7,8,9 -Tetrahydro-4-(trifluoromethyl)-1*H*,6*H*-pyrrolo[1',2':4,5][1,4]-oxazino[2,3-*f*]quinolin-2-one;

2,3,4,7-Tetrahydro-2,2,4-trimethyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-8-Chloro-3-ethyl-3,4-dihydro-8-isopropoxy-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-2*H*-[1,4]oxazino[2,3-*f*]quinoline;

(3*R*)-3-Ethyl-3,4-dihydro-8-isopropoxy-8-methoxy-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-2*H*-[1,4]oxazino[2,3-*f*]quinoline;

(±)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(–)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(+)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-4-methyl-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

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It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

(±)-4-Ethyl-2,3,4,7-tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(-)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(+)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-4-Cyclopropylmethyl-2,3,4,7-tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Cyclopropylmethyl-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-2-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-4-(2-hydroxy-2-methylpropyl)-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

(3*R*)-2,3,4,7-Tetrahydro-3-isobutyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

pharmaceutically acceptable salts thereof.

58. A compound selected from the group consisting of:

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

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CERTIFICATE OF CORRECTION

PATENT NO. .: 7,214,690

APPLICATION NO .: 10/080,503

DATED .: MAY 8, 2007

INVENTOR(S) .: HIGUCHI ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(7a*R*,10a*S*)-7-Ethyl-7,7a,8,9,10,10a-hexahydro-1-(trifluoromethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(±)-(2*S*,3*R*)-2,3,4,7-Tetrahydro-2,3-dimethyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(–)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

(+)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

pharmaceutically acceptable salts thereof.

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A Prospective Randomized Trial Comparing Low Dose Flutamide, Finasteride, Ketoconazole, and Cyproterone Acetate-Estrogen Regimens in the Treatment of Hirsutism

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ABSTRACT

Sixty-six hirsute women were randomized and treated with 1) flutamide (n = 15), 250 mg/day; 2) finasteride (n = 15), 5 mg/day; 3) ketoconazole (n = 16), 300 mg/day; and 4) ethinyl estradiol (EE)-cyproterone acetate (CPA; n = 20), 0.01 mg EE/day for the first week, 0.02 mg EE/day for the second week, and 0.01 mg EE/day for the third week, followed by a pause of 7 days, then 12.5 mg CPA/day added during the first 10 days of every month for 12 months. Hirsutism was evaluated by the Ferriman-Gallwey score, and hair diameter and hair growth rate were determined by a special image analysis processor in basal conditions and after 90, 180, 270, and 360 days of treatment. All treatments produced a significant decrease in the hirsutism score, hair diameter, and daily hair growth rate: flutamide, $-55 \pm 13\%$, $-21 \pm 14\%$, and $-37 \pm 18\%$; finasteride, $-44 \pm 13\%$, $-16 \pm 12\%$, and $-27 \pm 14\%$; ketoconazole, $-53 \pm 18\%$, $-14 \pm 12\%$, and $-30 \pm 21\%$; and EE-CPA, $-60 \pm 18\%$, $-20 \pm 11\%$, and $-28 \pm 21\%$.

Some differences existed among treatments with regard to effectiveness; EE-CPA and flutamide seem to be the most efficacious in improving hirsutism. For the hirsutism score, a greater decrease was seen with EE-CPA ($-60 \pm 18\%$) than with finasteride ($-44 \pm 13\%$; $P < 0.01$) and a greater decrease was seen with flutamide ($-58 \pm 18\%$) than with finasteride ($-44 \pm 13\%$; $P < 0.05$). Flutamide is the fastest in decreasing hair diameter; EE-CPA is the fastest in slowing down hair growth, even though at the end of the treatment there was a significant difference between flutamide and finasteride only ($-41 \pm 18\%$ *vs.* $-27 \pm 14\%$; $P < 0.05$).

Flutamide, ketoconazole, and EE-CPA induced a significant decrease in total and free testosterone, 5α-dihydrotestosterone, dehydroepiandrosterone, dehydroepiandrosterone sulfate, and androstenedione plasma levels. During the EE-CPA treatment, gonadotropins were suppressed, and the sex hormone-binding globulin level increased. Finasteride induced a decrease in dehydroepiandrosterone sulfate and 5α-dihydrotestosterone and an increase in testosterone levels.

Very few side-effects were observed during treatment with low doses of flutamide, EE-CPA, and particularly finasteride. Flutamide induced a decrease whereas EE-CPA induced an increase in triglycerides and cholesterol, showing higher values within the normal range. Ketoconazole induced several side-effects and complications, and several people dropped out of the study.

Despite different modalities of action and significantly different effects on androgen levels, low doses of flutamide, finasteride, and EE-CPA constitute very satisfactory alternative therapeutic regimens in the treatment of hirsutism. (*J Clin Endocrinol Metab* **84:** 1304–1310, 1999)

FLUTAMIDE (1–5), finasteride (6–10), ketoconazole (11–14), and cyproterone acetate (CPA) (15–20) are commonly employed in the treatment of hirsutism. Different therapeutic regimens have been used successfully; however, only a few randomized controlled trials exist, and subjective methods of evaluation are generally employed.

The aim of the present report was to compare, in a prospective, comparative, randomized study, as objectively as possible, the therapeutic efficacy as well as the endocrine and metabolic effects and reliability of low dose regimens of flutamide, finasteride, ketoconazole, and a combination of CPA and ethinyl estradiol (EE).

Subjects and Methods

Sixty-six premenopausal hirsute women (mean ± SD age, 22.9 ± 4.7) were referred to the Reproductive Medicine Unit of the University of Bologna (Bologna, Italy) for evaluation and treatment of hirsutism. The mean ± SD body weight was 61 ± 10 kg, and the mean ± SD height was 163 ± 6 cm. The mean body mass index (BMI) was 22.7 ± 2.7 (normal range, 18–24); 11 subjects (16%) were overweight (mean BMI, 27 ± 2.6).

Regular menses were reported by 29 of the 66 women; 32 had oligomenorrhea, 3 had amenorrhea, and 2 had polymenorrhea. Thirty-eight patients (58%) had ovulatory cycles (on the basis of typical progesterone levels in the premenstrual phase), and 28 (42%) had anovulatory cycles. Each patient underwent a complete medical and gynecological examination. In accordance with our codified parameters (21), all subjects had an etiological diagnosis of hirsutism. None of the women gave evidence of a hormonally active adrenal gland, an ovarian tumor, or Cushing's, PRL, or thyroid disorder. Twenty-seven patients (41%) had a diagnosis of polycystic ovary syndrome; 18 had anovulatory or oligoovulatory cycles, elevated plasma LH concentrations (LH/FSH ratio >2), high levels of testosterone and androstenedione, and ecographic evidence of enlarged polycystic ovaries. Nine patients had the concomitant presence of high dehydroepiandrosterone sulfate levels. Fourteen hirsute patients (21%) suffered from a mild form of nonclassic adrenal hyperplasia with high 17α-hydroxyprogesterone values, as diagnosed by ACTH test (21). Twenty-five patients (38%) were classified as having idiopathic hirsutism because they did not present any of the clinical features found in the other groups and had ovulatory cycles. In the entire population studied the hirsutism score ranged from 7–22.

Patients were randomized into four groups for treatment, indepen-

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Attorney's Docket No.: 18202-018001 / 1082

RESPONSE UNDER 37 CFR §1.116 -- EXPEDITED PROCEDURE -- EXAMINING GROUP 1600

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Lin Zhi *et al.* Art Unit : 1623
Serial No. : 10/080,503 Examiner : Lawrence E. Crane, Ph.D.
Filed : February 22, 2002
Title : **TRICYCLIC QUINOLINONE AND TRICYCLIC QUINOLINE ANDROGEN RECEPTOR MODULATOR COMPOUNDS AND METHOD**

MAIL STOP AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE AFTER FINAL

Dear Sir:

Responsive to the Final Office Action, mailed January 25, 2006, entry and consideration of the following amendments and remarks are respectfully requested. It is respectfully submitted that the amendments and arguments presented below either place the application into condition for allowance or reduce the number of issues for appeal. For example, claims 1 and 58 are amended to define the substituents of the optionally substituted groups, obviating the rejections under 35 U.S.C. 112, first and second paragraphs. Claims 1 and 58 also are amended to separate the substituents for variables X and Z, as suggested by the Examiner in the rejection under 35 U.S.C. 112, first paragraph. Claims 1, 9, 29-31, 49, 50, 58, 63, 71 and 72 are amended to cancel subject matter directed to substituents that when taken together form a carbocyclic or heterocyclic ring, obviating the rejection under 35 U.S.C. 112, first paragraph.

Amendments to the claims are reflected in the listing of the claims which begin on page 2 of this paper.

Remarks/Arguments begin on page 22 of this paper.

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Stephanie Seidman

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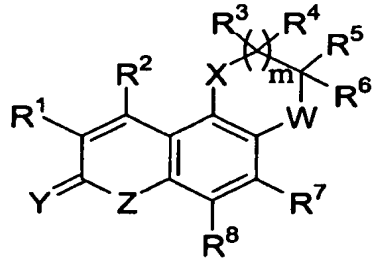
AMENDMENTS TO THE CLAIMS:

Claims 1-9, 11-31, 37-40, 46, 49-51, 56-72, 75-77 and 108 are pending. Claims 10, 41, 42 and 45 are cancelled herein without prejudice or disclaimer. Please amend claims 1, 9, 29-31, 49-51, 58, 63, 71, 72, 76 and 77 as indicated. New claim 108 is added herein. This listing of claims will replace all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1. (Currently amended) A compound having the formula:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl;

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl; ~~or~~

~~R^3 and R^4 taken together form a three to eight membered saturated or unsaturated carbocyclic or heterocyclic ring; or~~

~~R^3 and R^5 taken together form a three to eight membered saturated or unsaturated carbocyclic ring; or~~

~~R^3 and R^6 taken together form a three to eight membered saturated or unsaturated carbocyclic ring; or~~

~~R^3 and R^{13} taken together form a three to eight membered saturated or unsaturated heterocyclic ring;~~

R^5 and R^6 each independently is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl; ~~or~~

~~R^5 and R^6 taken together form a three to eight membered saturated or unsaturated carbocyclic ring; or~~

~~R^5 and R^{13} taken together form a three to eight membered saturated or unsaturated heterocyclic ring; or~~

~~R^6 and R^{13} taken together form a three to eight membered saturated or unsaturated heterocyclic ring;~~

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{10} is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl,

optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{13} is selected from the group consisting of optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_2 - C_8$ alkenyl, optionally substituted $C_2 - C_8$ alkynyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl;

m is selected from the group consisting of 0, 1 and 2;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of ~~$S(O)_n$~~, NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X ~~and Z each independently~~ is ~~selected from the group consisting of~~ O; ~~, NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$;~~

Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof; wherein:

the substituents of an optionally substituted group comprise one or more substituents independently selected from among alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyester, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9, $NR^{10}R^{11}$, CF_2CF_3, CH_2CH_2F and CH_2CF_3.

2. (Previously presented) A compound according to claim 1, wherein R^1 is selected from the group consisting of hydrogen, F, Cl, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

3. (Previously presented) A compound according to claim 2, wherein R^1 is selected from the group consisting of hydrogen, F, Cl, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

4. (Previously presented) A compound according to claim 3, wherein R^1 is selected from the group consisting of hydrogen, F and optionally substituted $C_1 - C_4$ alkyl.

5. (Previously presented) A compound according to claim 1, wherein R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl.

6. (Previously presented) A compound according to claim 5, wherein R^2 is selected from the group consisting of hydrogen, F, Cl, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

7. (Previously presented) A compound according to claim 6, wherein R^2 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_2$ alkyl, optionally substituted $C_1 - C_2$ haloalkyl and optionally substituted $C_1 - C_2$ heteroalkyl.

8. (Original) A compound according to claim 7, wherein R^2 is CF_3.

9. (Currently amended) A compound according to claim 1, wherein

R^3 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$~~; or~~

~~R^3 and R^6 taken together form a three to eight membered saturated or unsaturated carbocyclic ring~~.

Claim 10. (Cancelled)

11. (Previously presented) A compound according to claim 9, wherein R^3 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

12. (Previously presented) A compound according to claim 1, wherein R^6 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 -$

C_6 alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl.

13. (Previously presented) A compound according to claim 12, wherein R^6 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl, optionally substituted $C_1 - C_4$ heteroalkyl, optionally substituted $C_2 - C_4$ alkynyl and optionally substituted $C_2 - C_4$ alkenyl.

14. (Previously presented) A compound according to claim 13, wherein R^6 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

15. (Previously presented) A compound according to claim 12, wherein R^6 is selected from the group consisting of optionally substituted aryl, optionally substituted arylalkyl and optionally substituted heteroaryl.

16. (Previously presented) A compound according to claim 1, wherein R^5 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkynyl, optionally substituted $C_2 - C_6$ alkenyl.

17. (Previously presented) A compound according to claim 16, wherein R^5 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl and optionally substituted $C_1 - C_6$ heteroalkyl.

18. (Previously presented) A compound according to claim 17, wherein R^5 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

19. (Original) A compound according to claim 18, wherein R^5 is hydrogen or CF_3.

20. (Previously presented) A compound according to claim 1, wherein R^7 is selected from the group consisting of hydrogen, F, Cl, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

21. (Previously presented) A compound according to claim 1, wherein R^8 is selected from the group consisting of hydrogen, F, Cl, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

22. (Original) A compound according to claim 21, wherein R^7 and R^8 are each hydrogen or optionally substituted $C_1 - C_2$ alkyl.

23. (Previously presented) A compound according to claim 1, wherein R^9 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl and optionally substituted $C_1 - C_6$ heteroalkyl.

24. (Previously presented) A compound according to claim 23, wherein R^9 is selected from the group consisting of hydrogen and optionally substituted $C_1 - C_4$ alkyl.

25. (Previously presented) A compound according to claim 1, wherein R^{10} is selected from the group consisting of hydrogen, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, CO_2R^{12}, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl and optionally substituted $C_1 - C_6$ heteroalkyl.

26. (Previously presented) A compound according to claim 25, wherein R^{10} is selected from the group consisting of hydrogen, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$ and CO_2R^{12}.

27. (Previously presented) A compound according to claim 1, wherein R^4 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

28. (Previously presented) A compound according to claim 27, wherein R^4 is selected from the group consisting of hydrogen and optionally substituted $C_1 - C_2$ alkyl.

29. (Currently amended) A compound according to claim 1, wherein R^{13} is selected from the group consisting of CF_3, CF_2Cl, CF_2H, CFH_2, CH_2CF_3, CH_2CF_2Cl, CH_2CCl_2F, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_3 - C_6$ cycloalkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkenyl, optionally substituted $C_2 - C_6$ alkynyl, optionally substituted aryl,

optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl~~; or~~

~~R^6 and R^{13} taken together form a five to seven membered saturated or unsaturated heterocyclic ring~~.

30. (Currently amended) A compound according to claim 29, wherein R^{13} is selected from the group consisting of CF_3, CF_2Cl, CF_2H, CFH_2, CH_2CF_3, CH_2CF_2Cl, CH_2CCl_2F, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl, optionally substituted $C_1 - C_4$ heteroalkyl, optionally substituted $C_2 - C_4$ alkenyl and optionally substituted aryl~~; or~~

~~R^6 and R^{13} taken together form a five to six membered saturated or unsaturated heterocyclic ring~~.

31. (Currently amended) A compound according to claim 30, wherein R^{13} is selected from the group consisting of CF_3, CF_2Cl, CF_2H, CFH_2, CH_2CF_3, CH_2CF_2Cl, CH_2CCl_2F, methyl, ethyl, propyl, isopropyl, isobutyl, cyclopropylmethyl, allyl~~; or~~

~~R^6 and R^{13} taken together form a five membered saturated or unsaturated heterocyclic ring~~.

Claims 32 – 36 (Cancelled).

37. (Original) A compound according to claim 1, wherein m is 0 or 1.

38. (Original) A compound according to claim 37, wherein m is 1.

39. (Currently amended) A compound according to claim 1, wherein W is selected from the group consisting of NH, $N\{R^{13}\}$ and $N\{C(Y)R^{11}\}$. ~~, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$.~~

40. (Original) A compound according to claim 39, wherein W is NH or $N\{R^{13}\}$.

Claims 41 and 42 (Cancelled).

Claims 43 and 44 (Cancelled).

Claim 45. (Cancelled).

46. (Original) A compound according to claim 45, wherein Z is NH or $N\{R^{11}\}$.

Claims 47 and 48 (Canceled).

49. (Currently amended) A compound according to claim 1, wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl;

R^3 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$; ~~or~~

~~R^3 and R^6 taken together form a three to eight membered saturated or unsaturated carbocyclic ring;~~

R^5 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl; and

R^6 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl; ~~or~~

~~R^6 and R^{13} taken together form a five to seven membered saturated or unsaturated heterocyclic ring~~.

50. (Currently amended) A compound according to claim 49, wherein:

R^7 is selected from the group consisting of hydrogen, F, Cl, optionally substituted C_1–C_4 alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl;

R^8 is selected from the group consisting of hydrogen, F, Cl, optionally substituted C_1–C_4 alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl; and

R^{13} is selected from the group consisting of CF_3, CF_2Cl, CF_2H, CFH_2, CH_2CF_3, CH_2CF_2Cl, CH_2CCl_2F, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$

haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_3 - C_6$ cycloalkyl, optionally substituted $C_2 - C_6$ alkenyl, optionally substituted $C_2 - C_6$ alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl~~; or~~

~~R^6 and R^{13} taken together form a five to seven membered saturated or unsaturated heterocyclic ring~~.

51. (Currently amended) A compound according to claim 50, wherein:

m is 0 or 1;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is ~~selected from the group consisting of~~ O~~; , S, NH and N{R^{11}};and~~

Z is ~~selected from the group consisting of NH,~~ NH or $N\{R^{11}\}$ ~~and O~~.

Claims 52 – 55 (Cancelled).

56. (Previously presented) A compound selected from the group consisting of:

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3,4-dimethyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-4-Ethyl-2,3,4,7-tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-4-Allyl-2,3,4,7-tetrahydro-3-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3,4-Diethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one ;

(3*R*)-4-Allyl-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-isobutyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-3-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-4-methyl-3-propyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R/S*)-4-Ethyl-2,3,4,7-tetrahydro-3-propyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R/S*)-2,3,4,7-Tetrahydro-3-propyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-methyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-4-Ethyl-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Allyl-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino-[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-phenyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-phenyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Cyclopropylmethyl-2,3,4,7-tetrahydro-3-phenyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Benzyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

2,3,4,7-Tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7-Ethyl-7,7a,8,9,10,10a-hexahydro-1-(trifluoromethyl)-4*H*-cyclopenta-[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-3-isopropoxy-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(±)-(2*S*,3*R*)-2,3,4,7-Tetrahydro-2,3-dimethyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(6a*R*)-6a,7,8,9 -Tetrahydro-4-(trifluoromethyl)-1*H*,6*H*-pyrrolo[1',2':4,5][1,4]-oxazino[2,3-*f*]quinolin-2-one;

2,3,4,7-Tetrahydro-2,2,4-trimethyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]-quinolin-8-one;

(3*R*)-8-Chloro-3-ethyl-3,4-dihydro-8-isopropoxy-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-2*H*-[1,4]oxazino[2,3-*f*]quinoline;

(3*R*) -3-Ethyl-3,4-dihydro-8-isopropoxy-8-methoxy-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-2*H*-[1,4]oxazino[2,3-*f*]quinoline;

(±)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(–)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(+)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-4-methyl-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-4-Ethyl-2,3,4,7-tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(-)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(+)-2,3,4,7-Tetrahydro-3,4-bis(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-4-Cyclopropylmethyl-2,3,4,7-tetrahydro-3-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-Cyclopropylmethyl-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(±)-2,3,4,7-Tetrahydro-2-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-4-(2-hydroxy-2-methylpropyl)-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isobutyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

a pharmaceutically acceptable salt thereof.

57. (Previously presented) A compound selected from the group consisting of:

(3*R*)-2,3,4,7-Tetrahydro-3-methyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-3-Ethyl-2,3,4,7-tetrahydro-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-3-ethyl-2,3,4,7-tetrahydro-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-2,3,4,7-Tetrahydro-3-isopropyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2-Chloro-2,2-difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(3*R*)-4-(2,2-Difluoroethyl)-2,3,4,7-tetrahydro-3-isopropyl-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(7a*R*,10a*S*)-7-Ethyl-7,7a,8,9,10,10a-hexahydro-1-(trifluoromethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(7a*R*,10a*S*)-7,7a,8,9,10,10a-Hexahydro-1-(trifluoromethyl)-7-(2,2,2-trifluoroethyl)-4*H*-cyclopenta[5,6][1,4]oxazino[2,3-*f*]quinolin-3-one;

(±)-(2*S*,3*R*)-2,3,4,7-Tetrahydro-2,3-dimethyl-4-(2,2,2-trifluoroethyl)-10-(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

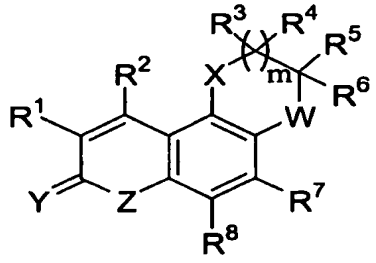
(±)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(–)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one;

(+)-2,3,4,7-Tetrahydro-4-(2,2,2-trifluoroethyl)-3,10-bis(trifluoromethyl)-8*H*-[1,4]oxazino[2,3-*f*]quinolin-8-one; and

a pharmaceutically acceptable salt thereof.

58. (Currently amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of formula:



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl;

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl; ~~or~~

~~R^3 and R^4 taken together form a three to eight membered saturated or unsaturated carbocyclic or heterocyclic ring; or~~

~~R^3 and R^5 taken together form a three to eight membered saturated or unsaturated carbocyclic ring; or~~

~~R^3 and R^6 taken together form a three to eight membered saturated or unsaturated carbocyclic ring; or~~

~~R^3 and R^{13} taken together form a three to eight membered saturated or unsaturated heterocyclic ring;~~

R^5 and R^6 each independently are selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_8$ alkynyl and optionally substituted $C_2 - C_8$ alkenyl; ~~or~~

~~R^5 and R^6 taken together form a three to eight membered saturated or unsaturated carbocyclic ring; or~~

~~R^5 and R^{13} taken together form a three to eight membered saturated or unsaturated heterocyclic ring; or~~

~~R^6 and R^{13} taken together form a three to eight membered saturated or unsaturated heterocyclic ring;~~

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ optionally substituted heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{10} is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted aryl, optionally substituted heteroaryl and optionally substituted arylalkyl;

R^{13} is selected from the group consisting of optionally substituted $C_1 - C_8$ alkyl, optionally substituted $C_1 - C_8$ haloalkyl, optionally substituted $C_1 - C_8$ heteroalkyl, optionally substituted $C_2 - C_8$ alkenyl, optionally substituted $C_2 - C_8$ alkynyl, optionally substituted $C_3 - C_8$ cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl;

m is selected from the group consisting of 0, 1 and 2;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of ~~$S(O)_n$~~, NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

~~X and Z each independently is selected from the group consisting of O; , NH, N{R^{11}}, N{C(Y)R^{11}}, N{SO_2R^{12}} and N{S(O)R^{12}};~~

Z is selected from the group consisting of NH, N{R^{11}}, N{C(Y)R^{11}}, N{SO_2R^{12}} and N{S(O)R^{12}}; and

Y is O;

and pharmaceutically acceptable salts thereof; wherein:

the substituents of an optionally substituted group comprise one or more substituents independently selected from among alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyester, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9, $NR^{10}R^{11}$, CF_2CF_3, CH_2CH_2F and CH_2CF_3.

59. (Original) A pharmaceutical composition according to claim 58, wherein said composition is suitable for enteral, parenteral, suppository or topical administration.

60. (Previously presented) A pharmaceutical composition according to claim 58, wherein R^1 is selected from the group consisting of hydrogen, F, Cl, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

61. (Previously presented) A pharmaceutical composition comprising a compound according to claim 1, wherein R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl.

62. (Previously presented) A pharmaceutical composition according to claim 59, wherein:

R^1 is selected from the group consisting of hydrogen, F and optionally substituted $C_1 - C_4$ alkyl; and

R^2 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_2$ alkyl, optionally substituted $C_1 - C_2$ haloalkyl and optionally substituted $C_1 - C_2$ heteroalkyl.

63. (Currently amended) A pharmaceutical composition according to claim 58, wherein R^3 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$, ~~; or~~

~~R^3 and R^6 taken together form a three to eight membered saturated or unsaturated carbocyclic ring.~~

64. (Previously presented) A pharmaceutical composition according to claim 58, wherein R^6 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl.

65. (Previously presented) A pharmaceutical composition according to claim 64, wherein R^6 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl, optionally substituted $C_1 - C_4$ heteroalkyl, optionally substituted $C_2 - C_4$ alkynyl and optionally substituted $C_2 - C_4$ alkenyl.

66. (Previously presented) A pharmaceutical composition according to claim 58, wherein R^5 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkynyl and optionally substituted $C_2 - C_6$ alkenyl.

67. (Previously presented) A pharmaceutical composition according to claim 66, wherein R^5 is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

68. (Previously presented) A pharmaceutical composition according to claim 58, wherein R^7 and R^8 each independently is selected from the group consisting of hydrogen, F, Cl, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

69. (Previously presented) A pharmaceutical composition according to claim 58, wherein:

R^9 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, and optionally substituted $C_1 - C_6$ heteroalkyl; and

R^{10} is selected from the group consisting of hydrogen, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, CO_2R^{12}, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl and optionally substituted $C_1 - C_6$ heteroalkyl.

70. (Previously presented) A pharmaceutical composition according to claim 58, wherein R^4 is selected from the group consisting of hydrogen, optionally substituted $C_1 - C_4$ alkyl, optionally substituted $C_1 - C_4$ haloalkyl and optionally substituted $C_1 - C_4$ heteroalkyl.

71. (Currently amended) A pharmaceutical composition according to claim 58, wherein R^{13} is selected from the group consisting of CF_3, CF_2Cl, CF_2H, CFH_2, CH_2CF_3, CH_2CF_2Cl, CH_2CCl_2F, optionally substituted $C_1 - C_6$ alkyl, optionally substituted $C_1 - C_6$ haloalkyl, optionally substituted $C_1 - C_6$ heteroalkyl, optionally substituted $C_2 - C_6$ alkenyl, optionally substituted $C_2 - C_6$ alkynyl, optionally substituted $C_3 - C_6$ cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted arylalkyl and optionally substituted heteroarylalkyl~~; or~~

~~R^6 and R^{13} taken together form a five to seven membered saturated or unsaturated heterocyclic ring~~.

72. (Currently amended) A pharmaceutical composition according to claim 71, wherein R^{13} is selected from the group consisting of CF_3, CF_2Cl, CF_2H, CFH_2, CH_2CF_3, CH_2CF_2Cl, CH_2CCl_2F, methyl, ethyl, propyl, isopropyl, isobutyl, cyclopropylmethyl, and allyl~~; or~~

~~R^6 and R^{13} taken together form a five membered saturated or unsaturated heterocyclic ring~~.

Claims 73 and 74 (Canceled).

75. (Original) A pharmaceutical composition according to claim 58, wherein m is 0 or 1.

76. (Currently amended) A pharmaceutical composition according to claim 58, wherein:

W is selected from the group consisting of NH, ~~N{R^{13}},~~ N{R^{13}}and N{$C(Y)R^{11}$}; and ~~N{SO_2R^{11}}; and~~

X is ~~selected from the group consisting of~~ O, ~~, NH and N{R^{11}}.~~

77. (Currently amended) A pharmaceutical composition according to claim 58, wherein Z is ~~selected from the group consisting of NH, NH or~~ N{R^{11}}. ~~and O.~~

Claims 78 – 107 (Cancelled).

108. (New) The compound of claim 1, wherein:

R^1 is selected from the group consisting of hydrogen, F, Cl, Br, I, NO_2, OR^9, $NR^{10}R^{11}$, $S(O)_nR^9$, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, $C_3 - C_8$ cycloalkyl, aryl, arylalkyl, heteroaryl, $C_2 - C_8$ alkynyl and o $C_2 - C_8$ alkenyl;

R^2 is selected from the group consisting of hydrogen, F, Cl, Br, I, CF_3, CF_2Cl, CF_2H, CFH_2, CF_2OR^9, CH_2OR^9, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, $C_3 - C_8$ cycloalkyl, aryl, arylalkyl, heteroaryl, $C_2 - C_8$ alkynyl and $C_2 - C_8$ alkenyl;

R^3 and R^4 each independently is selected from the group consisting of hydrogen, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$, $C(Y)NR^{10}R^{11}$, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, $C_3 - C_8$ cycloalkyl, aryl, arylalkyl, heteroaryl, $C_2 - C_8$ alkynyl and $C_2 - C_8$ alkenyl;

R^5 and R^6 each independently is selected from the group consisting of hydrogen, CF_3, CF_2Cl, CF_2H, CFH_2, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, $C_3 - C_8$ cycloalkyl, aryl, arylalkyl, heteroaryl, $C_2 - C_8$ alkynyl and $C_2 - C_8$ alkenyl;

R^7 is selected from the group consisting of hydrogen, F, Cl, Br, I, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, aryl, heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^8 is selected from the group consisting of hydrogen, F, Cl, Br, I, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, aryl, heteroaryl, OR^9, $S(O)_nR^9$, $NR^{10}R^{11}$, $C(Y)OR^{11}$ and $C(Y)NR^{10}R^{11}$;

R^9 is selected from the group consisting of hydrogen, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, aryl, heteroaryl and arylalkyl;

R^{10} is selected from the group consisting of hydrogen, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, aryl, heteroaryl, arylalkyl, CO_2R^{12}, $C(O)R^{12}$, SO_2R^{12} and $S(O)R^{12}$;

R^{11} and R^{12} each independently is selected from the group consisting of hydrogen, $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, aryl, heteroaryl and arylalkyl;

R^{13} is selected from the group consisting of $C_1 - C_8$ alkyl, $C_1 - C_8$ haloalkyl, $C_1 - C_8$ heteroalkyl, $C_2 - C_8$ alkenyl, $C_2 - C_8$ alkynyl, $C_3 - C_8$ cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl;

m is selected from the group consisting of 0, 1 and 2;

n is selected from the group consisting of 0, 1 and 2;

W is selected from the group consisting of NH, $N\{R^{13}\}$, $N\{C(Y)R^{11}\}$ and $N\{SO_2R^{11}\}$;

X is O;

Z is selected from the group consisting of NH, $N\{R^{11}\}$, $N\{C(Y)R^{11}\}$, $N\{SO_2R^{12}\}$ and $N\{S(O)R^{12}\}$; and

Y is O;

and pharmaceutically acceptable salts thereof

REMARKS

A check for $120 for the fee for a one-month extension of time accompanies this response. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for extension of time is needed, this paper is to be considered such Petition. Supporting art accompanies this response.

Claims 1-9, 11-31, 37-40, 46, 49-51, 56-72, 75-77 and 108 are pending. Claims 10, 41, 42 and 45 are cancelled herein without prejudice or disclaimer. Applicant reserves the right to file a continuation application directed to cancelled subject matter. Claims 1, 9, 29-31, 49-51, 58, 63, 71, 72, 76 and 77 are amended herein to more distinctly claim the subject matter. Claims 1 and 58 are amended to define the substituents of the optionally substituted groups. Basis for the amendment is found throughout the specification (*e.g.*, see page 11, line 26 through page 12, line 9). Claims 1 and 58 also are amended to separate the substituents for variables X and Z. Claims 1, 9, 29-31, 49, 50, 58, 63, 71 and 72 are amended to cancel subject matter directed to substituents that when taken together form a carbocyclic or heterocyclic ring. Applicant reserves the right to file a continuation application directed to cancelled subject matter. Claims 51 and 76 are amended to more distinctly claim the substituents for X and Z. Basis for new claim 108 is found throughout the specification (for example, see pages 3-7 and original claim 1). No new matter is added.

THE REJECTION OF CLAIMS 1-31, 37-42, 45, 46, 49-51, 58-72 AND 75-77 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH – Scope of Enablement

Claims 1-31, 37-42, 45, 46, 49-51, 58-72 and 75-77 are rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter not described in the specification in such a way as to enable one of skill in the art to make and/or use the claimed subject matter. The Examiner states that the compound and pharmaceutical composition claims are only enabled in part because the instant claims include terms that allegedly are incompletely defined. The Examiner also alleges that it would require undue experimentation to practice the full scope of the claims. The Examiner alleges that "the scope is excessive in view of the disclosed exemplifications." Applicant respectfully traverses the rejection.

RELEVANT LAW

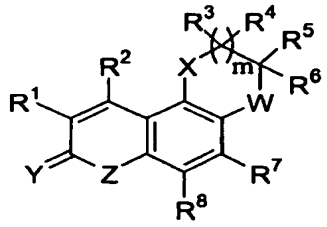
The test of enablement is whether one skilled in the art can make and use what is claimed based upon the disclosure in the application and information known to those of skill in the art without undue experimentation. *United States v. Telectronics, Inc.*, 8 USPQ2d

1217 (Fed. Cir. 1988). A certain amount of experimentation is permissible as long as it is not undue. A patent application need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987). Indeed, "not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted." *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332. Showing every combination of substituents is unnecessary.

A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. *See, Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

THE CLAIMS

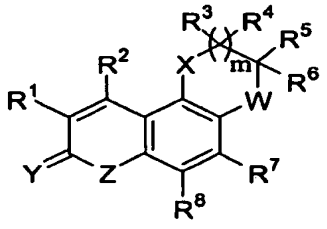
Claim 1 is directed to a compound having the formula:



(I)

where the substituents are as recited in the claims. Claims 2-9, 11-31, 37-40, 46 and 49-51 ultimately depend from claim 1 and are directed to various embodiments thereof.

Claim 58 is directed to a pharmaceutical composition that includes a pharmaceutically acceptable carrier and a compound of formula:



(I)

where the substituents are as recited in the claims. Claims 59-72, 75 and 76 ultimately depend from claim 58 and are directed to various embodiments thereof.

ANALYSIS

Applicant respectfully submits that the Examiner rejects claims 1-31, 37-42, 45, 46, 49-51, 58-72 and 75-77 under 35 U.S.C. § 112, first paragraph on page 2 and on page 3 of the Office Action. Both rejections state that the claims are rejected because it is alleged that practicing the full scope of the claims requires undue experimentation. Applicant respectfully requests that the Examiner clarify the difference between the rejection on page 2 and the rejection on page 3 of the Office Action so that Applicant can address the rejections with particularity. In order to be fully responsive, Applicant provides the following traverse.

The *In re Wands* factors

Applying the *In re Wands* factors to the instant facts reveals that the amount of experimentation is not undue. The analysis and arguments set forth in the previous responses of record are incorporated by reference herein.

a. The scope of the claims.

The pending claims recite compounds of Formula I and compositions thereof. The Examiner alleges that:

> The repeated use of the term "may be optionally substituted" without specifying the substituents implied thereby renders the breadth of the claim excessive because said term implies that the unnamed substituents is/are open to all possible alternatives.

First, the pending claims do not include the recitation "may be optionally substituted." The pending claims include the recitation "optionally substituted." Further, as discussed above, claims must be read in view of the specification. See *e.g.*, MPEP § 2106 ("An applicant is entitled to be his or her own lexicographer, and in many instances will provide an explicit definition for certain terms used in the claims. Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim."); MPEP § 608.01(o) ("The meaning of every term used in any of the claims should be apparent from the descriptive portion of the specification"); MPEP § 2173.05 ("When the specification states the meaning that a term in the claims is intended to have, the claim is examined using that meaning in order to achieve a complete exploration of the applicant's invention and its relation to the prior art."). The term "optionally substituted" is expressly defined in the specification. Thus, the recitation "optionally substituted" does not imply "that the unnamed substituents is/are open to all possible alternatives" as alleged by the Examiner. Thus, reciting that definition in the claims is not necessary. Without a acquiescing to the Examiner's allegation and solely to expedite issuance of the application, independent claims 1

and 58 are amended herein to recite the substituents encompassed by the recitation "optionally substituted" in the claims.

b. Nature of the Invention

The specification provides a general description of non-steroidal compounds that are high-affinity, high-specificity agonists, partial agonists (*i.e.*, partial activators and/or tissue-specific activators) and antagonists for androgen receptors (AR). The claimed subject matter is directed to androgen receptor modulator compounds and pharmaceutical compositions containing such compounds.

The Examiner states that the nature of the invention "includes a method of testing, a method of purification and a vast number of medicinal treatment[s] wherein compounds of instant claim 1 are administered to a host in need of such treatment." Applicant respectfully submits that the pending claims are directed to compounds as recited in the claims and to pharmaceutical compositions thereof. There currently are no method claims pending.

c. State of the Prior Art

Applicant respectfully submits that, at the time of the priority application, the mechanism of action of the intracellular receptors and the effects of small molecule agonists, antagonist or partial agonists on IR-mediated transcription modulation was well known to the skilled artisan (for example, see Rosen *et al.* (*J. Med. Chem.*, 1995, vol. 38, No. 25, pp 4855-4874, a copy of which is provided herein). Androgen receptor agonist compounds and their use as therapeutic agents also was known to those skilled in the medical arts. For example, Rosen *et al.* provides an overview of diseases and conditions that share mediation by androgen receptors as an underlying etiology. For example, Rosen *et al.* recites on page 4862:

> "Androgens are synthesized in the testes, adrenal cortex, and ovaries. The net effect of endogenous androgens reflects the combined actions of the secreted hormone, testosterone; its 5α-reduced metabolite, dihydrotestosterone; and its estrogenic derivative, estradiol. Androgens serve different functions at different stages of male development and have clear therapeutic uses in the treatment of hypogonadism, growth retardation, breast carcinoma, and osteoporosis. The actions of androgens are mediated through AR."

Applicant also submits that at the time of the priority application, androgen receptor agonist compounds were either in clinical trials or were available to the public for the treatment of hypogonadism, metastatic breast cancer, anemias, as anabolic agents and for the treatment of other diseases or conditions. For example, Testoderm®, a testosterone transdermal patch, was approved in the U.S. in 1993 for hormone replacement therapy in hypogonadal men. Androderm®, also a transdermal testosterone patch, was approved in the

U.S. in 1995 for the treatment of hypogonadism. Testred®, which contains the AR agonist methyltestosterone, was approved in the U.S. in 1973 for hormone replacement therapy in hypogonadal men as well as for the treatment of metastatic breast cancer in women. Anadrol®-50, which contains the AR agonist oxymetholone, was approved in the U.S. in 1972 and is used in the treatment of anemias caused by deficient red cell production. It also is well known that testosterone, the native androgen and AR agonist, is an anabolic agent. Therefore, it was well known in the prior art at the time of filing the original application that androgen receptor agonist compounds and compositions that include AR agonist compounds are useful in male hormone replacement therapy, in stimulation of hematopoiesis, as anabolic agents, and in the treatment of wasting diseases, hypogonadism and breast cancer.

Applicant also respectfully submits that, at the time of filing the priority application, the use of androgen receptor antagonists as therapeutic agents was known to those skilled in the medical arts. For example, Singh *et al.*, teaches that androgen receptor antagonists are useful for treating prostate cancer, acne, seborrhea, hirsuitism and androgenic alopecia (Singh *et al.*, Current Medicianl Chemistry 7: 211-247 (2000)). Rosen *et al.* (*J. Med. Chem.*, 1995, vol. 38, No. 25, pp 4855-4874) also provides an overview of diseases and conditions that share an etiology of being mediated by androgen receptor antagonists. For example, Rosen *et al.* recites on page 4862:

> "Compounds that block the action or synthesis of androgens have proven useful in treatment of diseases such as prostate cancer, prostatic hypertrophy, hirsutism, male pattern baldness, and acne. Among the most potent orally active anti-androgens is cyproterone acetate. This compound possesses progestational activity and suppresses the secretion of gonadotrphins, both of which are unwanted side effects. Other anti-androgens include flutamide, a prodrug for the active metabolite, 2-hydroxyflutamide, casodex, and an analogue of nilutamide."

Applicant also submits that at the time of filing the instant application, several androgen receptor antagonist compounds were either in clinical trials or were available to the public for the treatment of the diseases or conditions listed above. For example, Eulexin®, which contains the androgen receptor antagonist flutamide, was approved in the U.S. in 1989 for the treatment of prostate cancer. Casodex® (bicalutamide), an androgen receptor antagonist, was approved in 1995 for the treatment of prostate cancer. The AR antagonist cyproterone acetate was approved for use in Europe as early as 1978 for the treatment of female acne and hirsutism (Gruber *et al.*, Arch Dermatol 134: 459-463 (1998), Venturoli *et al*, J Clin Endocrinology & Metabolism 84(4): 1304-1310 (1999)).

In addition, a number of methods and assays for identifying agonists, partial agonists or antagonists of the steroid receptors was known at the time of filing the original application. For example, Berger *et al.* teaches a co-transfection assay (Berger *et al.*, J. Steroid Biochem. Molec. Biol. 41: 773 (1992)). Berger *et al.* teaches that activity in the co-transfection assay correlates very well with known *in vivo* activity, such that the co-transfection assay functions as a qualitative and quantitative predictor of a tested compounds *in vivo* pharmacology.

Thus, at the time of filing of the instant application, a broad body of knowledge had amassed in the areas of pharmaceutical sciences, medicine, and biochemistry directed to compounds that agonize or antagonize the steroid receptors, including androgen receptors, and to the use of compounds that agonize or antagonize the steroid receptors, such as androgen receptors, for treatment of diseases and conditions.

d. Level of Skill in the Art

As the Examiner noted, the skill in the art of chemical synthesis is high. That skill, together with the instant specification, including cited and incorporated references, allow the skilled artisan to make any and all of the claimed compounds. The Examiner states that "the level of skill in the medicinal arts is moderate because it is unclear which if any of the compounds disclosed herein are active against one or more specific disease conditions." Applicants respectfully disagree. The level of skill in the medical arts is independent of the issues. The skill of the medical practitioner does not vary.

Applicant respectfully submits that the level of skill in the medical arts is high. This is evidenced by the art in this area, which is authored primarily by those with Ph.D. and M.D. degrees and is intended for an audience of similarly highly skilled individuals, primarily in the fields of biochemical, pharmaceutical, or medical arts. The numerous articles and patents made of record in this application, authored and reviewed by those known in the art, address a highly skilled audience, and further evidence the high level of skill in this art. Therefore, the amount of disclosure required to meet the enablement requirement is minimal.

With respect to the rejection, it is respectfully submitted that no evidence is provided to support the Examiner's position that "the level of skill in the medicinal arts is moderate because it is unclear which if any of the compounds disclosed herein are active against one or more specific disease conditions." The Examiner is reminded that MPEP 2144.03 states:

> The Examiner may take official notice of facts outside of the record which are capable of instant and unquestionable demonstration as being "well- known" in the art. *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970). . . ..

The facts of which the Examiner is taking notice are conclusory and are not capable of instant and unquestionable demonstration as being "well-known" in the art. MPEP 2144.03 continues:

> If justified, the examiner should not be obliged to spend time to produce documentary proof. If the knowledge is of such notorious character that official notice can be taken, it is sufficient so to state. *In re Malcolm*, 129 F.2d 529, 54 USPQ 235 (CCPA 1942). If the applicant traverses such an assertion the examiner should cite a reference in support of his or her position.

If this position is maintained, the Examiner must provide a reference supporting this position.

e. Predictability of the Art

The Examiner alleges that the level of predictability in the art is indeterminate because it allegedly is not clear which compounds are active as androgen receptor agonists or antagonists. Applicant respectfully disagrees.

The instant application provides detailed teachings of *in vitro* and *in vivo* assays that allow one of skill in the art to test the compounds as instantly claimed for androgen receptor activity. The instant application, for example pages 110-114, provides a highly detailed teaching of *in vitro* assays, such as the "cis-trans" or "co-transfection" assay. Table 1 on page 115 of the specification provides *in vitro* binding data of exemplary compounds disclosed in the instant application that exhibit androgen receptor agonist activity, partial agonist activity, or antagonist activity. These assays are known in the art (see Evans *et al.*, Science 240: 889-95 (1988) and correlate well with *in vivo* activity and can function as a qualitative and quantitative predictor of a tested compounds *in vivo* pharmacology (Berger *et al.*, J. Steroid Biochem. Molec. Biol. 41: 773 (1992)). The data indicates that all of the exemplary compounds possess androgen receptor agonist, partial agonist or antagonist activity.

The compounds of the instant application are further characterized for their specificity for the androgen receptor by examining the *in vitro* binding activity with other members of the steroid receptors. Table 2 on page 116 provides binding data for exemplary compounds disclosed in the instant application with the androgen, progesterone, estrogen, glucocorticoid and mineralcorticoid receptors. As noted above, the androgen receptor agonist activity or antagonist activity shown in the *in vitro* assays correlates very well with *in vivo* activity. Once the androgen receptor activity of the compounds have been established, the application of those compounds to the treatment of any diseases responsive to androgen receptor agonists or antagonists, as discussed above, is well within the routine skills of those skilled in the art through reference to the present specification as well as the general and specialized knowledge of those working in this recognized field. Further, formulating such compounds into a

pharmaceutical composition and administration of such compositions to a subject is well known in the medical arts.

f. The amount of direction or guidance presented and the presence of working examples

The Examiner admits that the specification discloses 150 exemplary compounds that are precursors, intermediates or final products of the claimed compounds. The specification also teaches seven generic synthesis schemes (for example, see page 33, 35, 37, 38, 39, 41 and 42). The application names over 150 exemplary AR modulator compounds (for example, see page 29 through 32 and claims 56 and 57). The specification also provides over 50 working examples and two screening assays. It is respectfully submitted that the direction provided by the specification is sufficient to allow one of skill in the art to synthesize, test and administer any and all compounds of the claimed subject matter. Modification of the reaction conditions or choice of starting materials is routine and within the scope of the teachings in the application and knowledge of one of skill in the art.

For example, Scheme I outlines the synthesis of 5-hydroxy-6-bromo-quinoline compounds **6** starting from a phenylenediamine derivative, for example, 5-chloro-1,3-phenylenediamine. Other phenylenediamine derivatives also can be used in the synthetic sequence outlined in Scheme I. For example, use of 5-chloro-1,4-phenylenediamine as the starting material in Scheme I results in the synthesis of 6-hydroxy-5-bromo-quinoline compounds.

Schemes III and V outline the synthesis of 7-nitro-1,4-benzoxazine compounds, which begin with the chemo- and regioselective N-alkylation of an amino alcohol onto a 3,4-dihalonitrobenzene, such as, for example, 3,4-difluoronitrobenzene. One of skill in the art would recognize that selective protection of the nitrogen atom of the aminoalcohol **13**, with, for example, di-tert-butyl dicarbonate, prior to reaction with 3,4-difluoronitrobenzene would result in the reaction of the alcohol moiety of the aminoalcohol at the 4-position of 3,4-difluoronitrobenzene. Removal of the protecting group on the nitrogen, with, for example, acid, followed by treatment with base would provide 6-nitro-1,4-benzoxazine compounds, which are regioisomers of structures **15** and **24**.

Scheme VI outlines a racemic route to 7-nitro-1,4-benzoxazine compounds **24** that begins with the *N*-alkylation of a 2-amino-5-nitrophenol by treatment with an aldehyde, its corresponding hydrate or hemiacetal, in the presence of a reducing agent, for example, sodium cyanoborohydride. However, use of a 2-amino-4-nitrophenol derivative as the starting material, instead of 2-amino-5-nitrophenol as depicted in Scheme VI, would provide 6-nitro-

1,4-benzoxazine compounds. 6-Nitro-1,4-benzoxazine compounds are regioisomers of compounds of structure **24**. One of skill in the art can readily follow these schemes or known variations of such schemes with any of a vast number of commonly available starting materials to arrive at the claimed subject matter. The art of chemical synthesis is predictable and is dictated by recognized chemical reactions and constraints. There is nothing of record to suggest that production or use of any of the claimed compounds or compositions would require development of new procedures or excessive experimentation. Organic synthesis methods have been used for decades. Hence, any experimentation would be routine to the skilled artisan. Therefore, in view of the teachings of the specification, in combination with what was known at the time the priority application was filed, Applicant respectfully submits that the claimed compounds can be prepared predictably using the methods disclosed in the specification or that are known to those skilled in this art.

Similarly, one of skill in the art can assess the activity of any of the claimed compounds using the binding assay or the co-transfection assay, both of which are disclosed in the specification, though one of skill in the art can assess compounds using other known assays. Various screening assays for assessing the ability of a compound or composition to modulate the transcriptional ability of intracellular receptors are known to those of skill in the art, such as those described in U.S. Pat. Nos. 4,981,784, 5,071,773, 5,298,429, and 5,506,102 and in WO89/05355, WO91/06677, WO92/05447, WO93/11235, WO93/23431, WO94/23068, WO95/18380 and CA 2,034,220. Further, formulating such compounds into a pharmaceutical composition and administration of such compositions to a subject is well know in the medical arts. Thus, preparation and administration of pharmaceutical compounds also is predictable. Finally, administration of compounds is routine to one of skill in the medical arts. Thus, it is respectfully submitted that the direction provided by the specification is sufficient to allow one of skill in the art to synthesize, test and administer any and all compounds of the claimed subject matter. Therefore, Applicant respectfully submits that one skilled in the art can make and use what is claimed based upon the disclosure in the application and information known to those of skill in the art without undue experimentation.

g. The amount of experimentation required

There is nothing of record to suggest that production or use of any of the claimed compounds or compositions would require development of new procedures or excessive experimentation. Organic synthesis methods have been used for decades. As discussed above, bioassays for evaluating whether compounds are functional ligands for receptor

proteins were known in the art since at least 1991. Such assays are routine in this art and do not require excessive experimentation. Applicant notes that "a considerable amount of experimentation is permissible, if it is merely routine . . ." *In re Wands* 858 F.3d 731, 737 (Fed Cir. 1988).

CONCLUSION

In light of the scope of the claims, the nature of the claimed subject matter, the state of the prior art, the high level of skill of those in this art, the predictability of the art, the amount of direction and guidance presented in the specification, the presence of over 50 working examples, the low amount of experimentation required and the fact that any required experimentation is routine, Applicant respectfully submits that it would not require undue experimentation for a person skilled in the art to make and use the claimed compounds and compositions. Therefore, the specification is enabling for making and using the full scope of the claimed subject matter. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

REBUTTAL TO THE EXAMINER'S ARGUMENTS

1. "Disclosed Exemplifications"

The Examiner alleges that the scope is excessive in view of the "disclosed exemplifications." Applicant respectfully disagrees. The specification discloses androgen receptor modulator compounds, pharmaceutical compositions containing such compounds as well as methods of using such compounds and pharmaceutical compositions for modulating processes mediated by steroid receptors. The application discloses methods of making such compounds and pharmaceutical compositions, as well as intermediates used in their synthesis. The specification describes seven generic synthesis schemes (for example, see page 33, 35, 37, 38, 39, 41 and 42). One of skill in the art can readily follow these schemes or known variations of such schemes with any of a vast number of commonly available starting materials to arrive at the claimed subject matter. The application names over 150 exemplary AR modulator compounds (for example, see page 29 through 32 and claims 56 and 57. The specification also provides over 50 working examples. The application teaches *in vitro* assays, such as the "cis-trans" or "co-transfection" assay, for characterizing exemplary AR modulator compounds. The specification provides *in vitro* binding data of exemplary compounds disclosed in the instant application that exhibit androgen receptor agonist activity, partial agonist activity, or antagonist activity. The compounds of the instant application are further characterized for their specificity for the androgen receptor by examining the *in vitro* binding activity with other members of the

steroid receptors. Hence the specification provides a variety of examples of compounds that fall within the scope of the claims evidencing that the claimed compounds function as claimed. The requirements of 35 U.S.C. §112, first paragraph, do not require a specific example of everything within the scope of the claims. *In re Anderson*, 176 USPQ 331, 333 (CCPA 1973) :

> ...we do not regard section 112, first paragraph, as requiring a specific example of everything within the scope of a broad claim . . . What the Patent Office is here apparently attempting is to limit all claims to the specific examples, not withstanding the disclosure of a broader invention. This it may not do.

In re Grimme, Keil and Schmitz, 124 USPQ 449, 502 (CCPA 1960) :

> It is manifestly impracticable for an applicant who discloses a generic invention to give an example of every species falling within it, or even to name every such species. It is sufficient if the disclosure teaches those skilled in the art what the invention is and how to practice it.

Hence there is no requirement for the applicant to exemplify or even provide an example of everything within the scope of the claims. The Patent Office cannot "limit all claims to the specific examples, notwithstanding the disclosure of a broader invention." A patentee's invention may be broader than the particular embodiment shown in the specification. A patentee not only is entitled to narrow claims particularly directed to the preferred embodiment, but also to broad claims that define the invention without a reference to specific instrumentalities. *Smith v. Snow*, 294 U.S. 1, 11, 24 USPQ 26, 30 (1935). Applicant is entitled to claims that are commensurate in scope not only with what applicant has specifically exemplified, but commensurate in scope with that which one of skill in the art could obtain by virtue of that which the applicant has disclosed.

2. "Defined by the Prior Art"

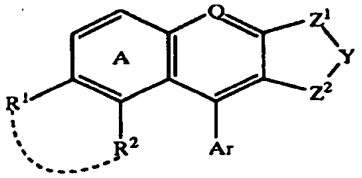
In the present Action, the Examiner alleges that "the state of the prior art is defined by the prior art presently cited by the Applicant and by Examiner and particularly by PTO-892 references F and G wherein anticipatory compounds and compositions have been disclosed." Applicant respectfully disagrees. The prior art is replete with references that show that the skilled artisan can use known organic synthesis schemes and reactions to produce various bicyclic, tricyclic and polycyclic organic compounds, including, for example, quinolines, quinolinones, coumarins, benzoxyzins, oxazolidines, azasteroids, progesterones, azachlormadinones, anthrasteroids, flutamides and phthalimides, and that the art of record teaches bioassays for evaluating whether compounds are functional ligands for receptor proteins and correlates the activity of ligands in such assays to *in vivo* activity (*e.g.*, see Evans *et al.* (US Pat. Nos. 4,981,784 and 5,071,773 and Science 240:889-95 (1988)).

Applicant disagrees that "the state of the prior art is defined by the prior art presently cited by applicant and by examiner." Applicant is not aware of such a definition and respectfully requests that the Examiner cite authority.

3. Alleged Anticipatory Prior Art

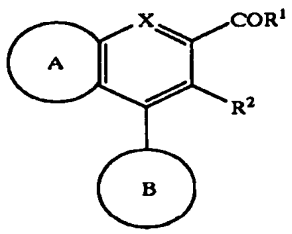
In the present Action, the Examiner alleges that certain references are anticipatory prior art (Action at page 4, which states that PTO-892 references F and G disclose anticipatory compounds and compositions). Reference F is US 6,030,967 (2/29/00) to Mauri *et al.* and Reference G is US 6,340,704 (1/22/02) to Mauri *et al.* Applicant respectfully submits that the Examiner has not rejected any of the claims under 35 U.S.C. § 102(b) as anticipated by either US Pat. Nos. 6,030,967 or 6,340,704. Applicant respectfully submits that neither US Pat. No. 6,030,967 nor US Pat. No. 6,340,704 discloses compounds as instantly claimed nor compositions thereof.

For example, US Pat. No. 6,030,967 discloses compounds having the formula:



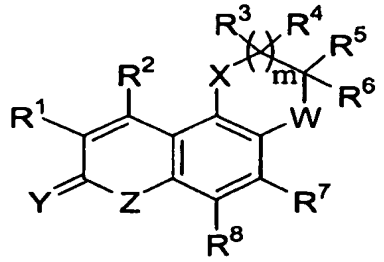
where Q is an optionally substituted carbon atom or $N(O)_p$ wherein p is 0 or 1; Y is an optionally substituted methylene group, $S(O)_q$ wherein q is an integer of 0 to 2, or an optionally substituted imino group; Z^1 is a C_{1-3} alkylene group which can have an oxo group or a thioxo group and can contain etherified oxygen or sulfur within the carbon chain; Z^2 is an optionally substituted C_{1-3} alkylene group; Ar is an optionally substituted carbocyclic group or an optionally substituted heterocyclic group; one of R^1 and R^2 is a hydrogen atom, a halogen atom, a hydroxyl group, an optionally substituted lower alkyl group, or an optionally substituted lower alkoxy group; the other is a halogen atom, a hydroxyl group, an optionally substituted lower alkyl group, or an optionally substituted lower alkoxy group; or R.sup.1 and R.sup.2 taken together with adjacent –c=c– form a ring; and ring *A* is a benzene ring which may be substituted in addition to R^1 and R^2 ; or a salt thereof.

US Pat. No. 6,340,704 discloses compounds having the formula:



where R^1 is an amino group that may be substituted, R^2 is a hydrogen atom or a lower alkyl group that may be substituted; X is a methane group that may be substituted or $N(O)_m$ (m is 0 or 1); ring *A* is a homo- or hetero-cycle that is substituted by a halogen atom, lower alkyl, lower alkoxy or lower alkylenedioxy group, and ring *B* is a homo- or hetero-cycle that may be substituted.

Neither US Pat. No. 6,030,967 nor US Pat. No. 6,340,704 discloses compounds or compositions as instantly claimed, such as those that have the structure set forth as formula I



I

and defined in the instant claims. Applicant also respectfully submits that the Office Action is internally inconsistent. At Paragraph C on Page 4 of the Action the Examiner alleges that PTO-892 References F and G disclose anticipatory compounds and compositions, while in Paragraph D on Page 4 of the Action, the Examiner states that these references disclose "many compounds very closely analogous to the instant claimed compounds." Further, on page 6 of the Action, the Examiner states that "claims 1-31, 37-42, 45, 46, 49-51, 58-72 and 75-77 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. 112" (see last sentence on page 6). Thus, it appears that the Examiner is mistaken when he states on page 4 of the Action that US Pat. No. 6,030,967 and US Pat. No. 6,340,704 disclose anticipatory compounds and compositions. In order to clarify the record of the instant prosecution history, Applicant respectfully requests that the Examiner withdraw the statement that US Pat. No. 6,030,967 and US Pat. No. 6,340,704 disclose anticipatory compounds and compositions.

4. The instant claims include terms that allegedly are incompletely defined

The Examiner alleges that the compounds and pharmaceutical composition claims are enabled only in part because the instant claims include terms that allegedly are incompletely defined. The prior Office Action raised this issue under 35 U.S.C. § 112, second paragraph, and it has not been maintained in the instant Action. Thus, it appears that the rejection under 35 U.S.C. § 112, second paragraph has been withdrawn. Notwithstanding this, in order to be fully responsive, Applicant respectfully traverses the rejection.

a. aryl

The Examiner alleges that the term "aryl" is incompletely defined because "said terms typically i) lack any upper bounds as to size." Applicant respectfully disagrees.

It is respectfully submitted that the specification specifically defines the term "aryl." For example, page 9, line 26 through page 10, line 5, recites:

> The term "aryl," alone or in combination, refers to an optionally substituted aromatic ring system. The term aryl includes monocyclic aromatic rings, polyaromatic rings and polycyclic aromatic ring systems containing from six to about twenty carbon atoms. The term aryl also includes monocyclic aromatic rings, polyaromatic rings and polycyclic ring systems containing from 6 to about 12 carbon atoms, as well as those containing from 6 to about 10 carbon atoms. The polyaromatic and polycyclic aromatic rings systems may contain from two to four rings. Examples of aryl groups include, without limitation, phenyl, biphenyl, naphthyl and anthryl ring systems.

This definition includes upper bounds as to size. Applicant respectfully submits that claims must be read in view of the specification. See, *e.g.*, MPEP § 2106 ("An applicant is entitled to be his or her own lexicographer, and in many instances will provide an explicit definition for certain terms used in the claims. Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim."); MPEP § 2173.05 ("When the specification states the meaning that a term in the claims is intended to have, the claim is examined using that meaning in order to achieve a complete exploration of the applicant's invention and its relation to the prior art."). The term "aryl" is expressly defined in the specification, and the definition recites specifics that the Examiner alleges to be missing ("bounds as to size"). Thus, the term "aryl" is not incompletely defined. Therefore, reciting the definition for "aryl" in the claims is not necessary.

b. arylalkyl

The Examiner alleges that the term "arylalkyl" is incompletely defined because "said terms typically i) lack any upper bounds as to size." Applicant respectfully disagrees. The term "arylalkyl" is defined in the specification. For example, see page 11, lines 9-11, which recites:

> The term "arylalkyl," alone or in combination, refers to an alkyl radical as defined above in which one hydrogen atom is replaced by an aryl radical as defined above, such as, for example, benzyl, 2-phenylethyl and the like.

The term "arylalkyl" is expressly defined in the specification, and references the terms "alkyl" and "aryl." As discussed above, the specification defines the recitation "aryl" (*e.g.*, see page 9, line 26 through page 10, line 5). In addition, the specification defines the recitation "alkyl" (*e.g.*, see page 8, lines 13-18):

> an optionally substituted straight-chain or branched-chain alkyl radical having from 1 to about 12 carbon atoms. The term also includes substituted straight-chain or branched-chain alkyl radicals having from 1 to about 6 carbon atoms as well as those having from 1 to about 4 carbon atoms. Examples of alkyl radicals include methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl, *tert*-butyl, *tert*-amyl, pentyl, hexyl, heptyl, octyl and the like.

The definitions provided in the specification for the terms "alkyl" and "aryl" recites the "upper bounds as to size" that the Examiner alleges to be missing. Thus, one of skill in the art would be apprised of the metes and bounds of the term "arylalkyl" when read in light of the specification. Therefore, reciting the definition for "arylalkyl" in the claims is not necessary.

c. heteroaryl

The Examiner alleges that the term "heteroaryl" is incompletely defined because:

> said terms typically
> i) lack any upper bounds as to size,
> and when heteroatoms are suggests said terms
> ii) fail to define which hetero atoms are to be selected from
> iii) the number of said heteroatoms, or
> iv) the location(s) or the ring system(s) containing said heteroatom(s) and
> v) because a proper definition of "optionally substituted" is not present in any independent claim.

Applicant respectfully submits that the specification defines the recitation "heteroaryl" (*e.g.*, see page 10, lines 6-19):

> optionally substituted aromatic ring systems containing from about five to about 20 skeletal ring atoms and having one or more heteroatoms such as, for example, oxygen, nitrogen and sulfur. The term heteroaryl also includes optionally substituted aromatic ring systems having from 5 to about 12 skeletal ring atoms, as well as those having from 5 to about 10 skeletal ring atoms. The term heteroaryl may include five- or six-membered heterocyclic rings, polycyclic heteroaromatic ring systems and polyheteroaromatic ring systems where the ring system has two, three or four rings. The terms heterocyclic, polycyclic heteroaromatic and polyheteroaromatic include ring systems containing optionally substituted heteroaromatic rings having more than one heteroatom as described above (*e.g.*, a six membered ring with two nitrogens), including polyheterocyclic ring systems of from two to four rings. The term heteroaryl includes ring systems such as, for example, furanyl, benzofuranyl, chromenyl, pyridyl, pyrrolyl, indolyl, quinolinyl, N-alkyl pyrrolyl, pyridyl-N-oxide, pyrimidoyl, pyrazinyl, imidazolyl, pyrazolyl, oxazolyl, benzothiophenyl, purinyl, indolizinyl, thienyl and the like.

The definition set forth in the specification for the term "heteroaryl" recites the "upper bounds as to size" that the Examiner alleges to be missing. The definition also states that the rings include one or more heteroatoms, such as oxygen, nitrogen and sulfur. Thus, Applicant respectfully submits that one of skill in the art, in light of what is known in the art and the teachings of the

specification, would understand what is meant by the recitation "heteroaryl" and would be able to determine the metes and bounds of the claims. Thus, reciting the definition for "heteroaryl" in the claims is not necessary.

d. "optionally substituted"

The term "optionally substituted" is defined in the specification at page 11, line 26 to page 12, line 9, which states:

> "Optionally substituted" groups may be substituted or unsubstituted. The substituents of an "optionally substituted" group may include, without limitation, one or more substituents independently selected from the following groups or designated subsets thereof: alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkoxy, aryloxy, haloalkoxy, amino, alkylamino, dialkylamino, alkylthio, arylthio, heteroarylthio, oxo, carboxyesters, carboxamido, acyloxy, hydrogen, F, Cl, Br, I, CN, NO_2, NH_2, N_3, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H, $C(O)NH_2$, OR^9, SR^9 and $NR^{10}R^{11}$. An optionally substituted group may be unsubstituted (e.g., $-CH_2CH_3$), fully substituted (e.g., $-CF_2CF_3$), monosubstituted (e.g., $-CH_2CH_2F$) or substituted at a level anywhere in-between fully substituted and monosubstituted (e.g., $-CH_2CF_3$).

Thus, the recitation "optionally substituted" does not imply "that the unnamed substituents is/are open to all possible alternatives" as alleged by the Examiner. As discussed above, claims must be read in view of the specification. Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. The term "optionally substituted" is expressly defined in the specification. Thus, reciting that definition in the claims is not necessary.

Furthermore, the USPTO recognizes the use of this term in patent claims. A search of the USPTO database for the time period 1976 to present for patents with the recitation "optionally substituted" in the claims yielded 22,359 patents. While applicant realizes that the prosecution history of one patent is not relevant to another, the widespread use of the recitation "optionally substituted" in claims evidences that one of skill in the art understands the meaning of this term.

Notwithstanding the above, without acquiescing to the Examiner's allegation and solely to expedite issuance of the application, independent claims 1 and 58 are amended herein to recite the substituents encompassed by the recitation "optionally substituted" in the claims.

5. Spiro structures

The Examiner alleges that no heterocyclic or homocyclic spiro examples are included in any of the synthetic schemes or any of the specific compounds in the application.

Without a acquiescing to the Examiner's allegation and solely to expedite prosecution, claim 10 is cancelled herein without prejudice or disclaimer and claims 1, 9, 29-31, 49, 50, 58, 63, 71 and 72 are amended to delete recitations where two particular substituents together form a carbocyclic or heterocyclic ring. Thus, the rejection is moot. Applicant expressly reserves the right to pursue the cancelled subject matter in a continuing application.

6. The definitions of variables X and Z

The Examiner suggests that the definitions of variables "X" and "Z" should be separated. Without a acquiescing to the Examiner's allegation and solely to expedite prosecution and advance the application to issuance, claims 1 and 58 are amended herein to define the variables "X" and "Z" separately.

REJECTION OF CLAIMS 1-7, 9, 11-18, 20-25, 27-30, 49, 58, 60-62, 64-71, 73 AND 74 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-7, 9, 11-18, 20-25, 27-30, 49, 58, 60-62, 64-71, 73 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention because the Examiner alleges that the recitation "optionally substituted" fails "to specify the substituents implied thereby." The Examiner also alleges that the definition for "optionally substituted" in the specification is "inadequate because the definition fails to meet the requirements of the statute for a variety of reasons noted in examiner's response following a previous rejection."

Applicant respectfully traverses the bases for the rejection in turn below.

RELEVANT LAW

Claims are not read in a vacuum but instead are considered in light of the specification and the general understanding of the skilled artisan. *Rosemount Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1547, 221 USPQ 1, 7 (Fed. Cir. 1984). Claim language is satisfactory if it reasonably apprises those of skill in the art of the bounds of the claimed invention and is as precise as the subject matter permits. *Shatterproof Glass Corp. v. Libby-Owens Ford Col.*, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir.), *cert. dismissed*, 106 S.Ct. 340 (1985).

ANALYSIS

"Optionally substituted"

As discussed above, the term "optionally substituted" is defined in the specification (*e.g.*, see page 11, line 26 to page 12, line 9). Claims must be read in view of the specification. Where an explicit definition is provided by the applicant for a term, that definition will control

interpretation of the term as it is used in the claim (see *e.g.*, MPEP § 2106). The term "optionally substituted" is defined in the specification and thus that definition will control interpretation of the claim. Thus, reciting the definition in the claims is not necessary.

Notwithstanding this, without a acquiescing to the Examiner's allegation and solely to expedite issuance of the application, independent claims 1 and 58 are amended herein to recite the substituents encompassed by the recitation "optionally substituted" in the claims.

Alleged "Inadequate" Definition

The Examiner does not distinctly recite the alleged deficiencies in the definition for the recitation "optionally substituted" provided in the specification. Applicant respectfully requests that the Examiner restate the rejection with particularity to afford the applicant an opportunity to properly respond. In order to be fully responsive, Applicant provides the following traverse.

The Examiner objects to the definition of "optionally substituted" recited in the specification because it includes the terms "aryl," "arylalkyl" and "heteroaryl" because:

said terms typically
i) lack any upper bounds as to size,
and when heteroatoms are suggests said terms
ii) fail to define which hetero atoms are to be selected from
iii) the number of said heteroatoms, or
iv) the location(s) or the ring system(s) containing said heteroatom(s) and
v) because a proper definition of "optionally substituted" is not present in any independent claim.

a. aryl

The specification specifically defines the term "aryl." For example, page 9, line 26 through page 10, line 5, recites:

> The term "aryl," alone or in combination, refers to an optionally substituted aromatic ring system. The term aryl includes monocyclic aromatic rings, polyaromatic rings and polycyclic aromatic ring systems containing from six to about twenty carbon atoms. The term aryl also includes monocyclic aromatic rings, polyaromatic rings and polycyclic ring systems containing from 6 to about 12 carbon atoms, as well as those containing from 6 to about 10 carbon atoms. The polyaromatic and polycyclic aromatic rings systems may contain from two to four rings. Examples of aryl groups include, without limitation, phenyl, biphenyl, naphthyl and anthryl ring systems.

This definition includes upper bounds as to size. Thus, the term "aryl" is not incompletely defined.

b. arylalkyl

The term "arylalkyl" is defined in the specification. For example, see page 11, lines 9-11, which recites:

> The term "arylalkyl," alone or in combination, refers to an alkyl radical as defined above in which one hydrogen atom is replaced by an aryl radical as defined above, such as, for example, benzyl, 2-phenylethyl and the like.

The terms "alkyl" and "aryl" are defined in the specification. As discussed above, the definition for the term "aryl" recites the "upper bounds as to size" that the Examiner alleges to be missing. Thus, the term "arylalkyl" is not incompletely defined.

c. heteroaryl

The specification defines the recitation "heteroaryl" (*e.g.*, see page 10, lines 6-19):

> optionally substituted aromatic ring systems containing from about five to about 20 skeletal ring atoms and having one or more heteroatoms such as, for example, oxygen, nitrogen and sulfur. The term heteroaryl also includes optionally substituted aromatic ring systems having from 5 to about 12 skeletal ring atoms, as well as those having from 5 to about 10 skeletal ring atoms. The term heteroaryl may include five- or six-membered heterocyclic rings, polycyclic heteroaromatic ring systems and polyheteroaromatic ring systems where the ring system has two, three or four rings. The terms heterocyclic, polycyclic heteroaromatic and polyheteroaromatic include ring systems containing optionally substituted heteroaromatic rings having more than one heteroatom as described above (*e.g.*, a six membered ring with two nitrogens), including polyheterocyclic ring systems of from two to four rings. The term heteroaryl includes ring systems such as, for example, furanyl, benzofuranyl, chromenyl, pyridyl, pyrrolyl, indolyl, quinolinyl, N-alkyl pyrrolyl, pyridyl-N-oxide, pyrimidoyl, pyrazinyl, imidazolyl, pyrazolyl, oxazolyl, benzothiophenyl, purinyl, indolizinyl, thienyl and the like.

The definition set forth in the specification for the term "heteroaryl" recites the "upper bounds as to size" that the Examiner alleges to be missing. The definition also states that the rings include one or more heteroatoms, such as oxygen, nitrogen and sulfur. Thus, Applicant respectfully submits that one of skill in the art, in light of what is known in the art and the teachings of the specification, would understand what is meant by the recitation "heteroaryl" and would be able to determine the metes and bounds of the claims. Thus, the term "heteroaryl" is not incompletely defined.

REBUTTAL TO THE EXAMINER'S ARGUMENTS

The Definition of Variable R^{18}

In the rejection under 35 U.S.C. 112, second paragraph, the Examiner alleges the recitation "may be optionally substituted" has been replaced with the recitation "optionally substituted" in the claims except in the case of variable R^{18} in claims 1 and 58. Without

addressing the propriety of the rejection, Applicant respectfully submits that neither claim 1 nor claim 58 recites a variable R^{18}. Thus, because claims 1 and 58 do not recite a variable R^{18}, this rejection is moot.

* * *

In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

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Notice of Allowability

Application No.	Applicant(s)	
10/080,503	HIGUCHI ET AL.	
Examiner	**Art Unit**	
L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed May 19, 2006*.

2. ☒ The allowed claim(s) is/are *1-31,37-40,46,49-51,56-72,76,77 and 108*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☒ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 4/5/05(update)
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *08232006* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☒ Other *PTO-1449 of 02/01/2006*

L. E. Crane, Ph.D., Esq.
Primary Patent Examiner
Technology Center 1600

Applicant is respectfully requested to supply an amended declaration because the handwritten alterations to the oath by inventor Caferro were not properly initialed and dated.

An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.

In claim **46**, the term "claim **45**" was amended to read
-- claim **1** --.

In claim **56** at line 108, the term -- and --was added at the end of the line.

In claim **56** at line 111, the term "a pharmaceutically acceptable salt" was amended to read -- pharmaceutically acceptable salts --.

In claim **57** at line 25, the term -- and -- was added at the end of the line.

In claim **57** at line 28, the term "a pharmaceutically acceptable salt" was amended to read -- pharmaceutically acceptable salts --.

In claim **58** at line 67, the entire line was deleted in favor of the term -- m is 1; --.

Claim **75** was cancelled.

In claim **108** at line 4, the term "and o" was amended to read
-- and --.

Authorization for this Examiner's Amendment was given in a telephone interview with Frank Miskiel on August 21, 2006

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

All Post-Allowance Correspondence concerning this application must be mailed to:

BOX ISSUE FEE
COMMISSIONER FOR PATENTS
WASHINGTON, DC 20231

OR you can FAX them to the Office of Patent Publications at 571-273-8300, in order to expedite the handling of such correspondence as amendments under 37 C.F.R. §1.312; Information Disclosure Statements (IDS's), and formal drawings. Sending Post-Allowance papers to Technology Center 1600 will only cause delays in matching papers with the case.

For information concerning status of correspondence sent after receipt of the Notice of Allowance, please contact the Correspondence Branch at **571-272-4200**. The Notice of Allowance also has an insert containing contact information for other items, including Issue Fees, receipt of formal drawings, and the status of the application.

LECrane:lec
08/23/2006

L. E. Crane, Ph.D. Esq.
Primary Patent Examiner
Technology Center 1600